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Dear Frank:

It amazes me that we haven't run into each other during the last eight years, considering that we've gravitated to the same midwestern region, and to not very different research interests. This gravitational attraction is continuing, at least to the extent that I've started a minor project on actinomycete genetics. This has been a bit of fun for me: I hardly knew what an actinomycete looked like a few weeks ago, and learning something new is always stimulating.

Anyhow, the experiments so far are very encouraging. Nutritional mutants (mostly for amino acids) proved to be rather easy to find, from UV-treated spores of S. griseus. When different nutritional mutants are cross-streaked on minimal agar, many of them coact to give prototrophic growth. This probably represents heterokaryon formation: most of the spores produced are one or the other mutant type. However, a few stable prototrophs also come out, and these may represent recombinations from a sexual phase. It will take some more looking-into to test this hypothesis properly. I had thought the literature on sexuality in eubacteria was confusing, but the actinomycete morphological work has it beat. The current experiments, if they mean anything, do not agree with any of the morphological accounts of sexual processes, or for that matter, with the more usually expressed refutation of any such mechanism.

In continuing these experiments, I'd like to try some related species. The diagnostic criteria usually applied (especially pigmentation) do not appear to be of fundamental biological significance, so that if intraspecific crossing is possible (and don't quote me yet that it is), species crosses should not be much more of a trick. For technical reasons, I need types that will grow readily on the same synthetic medium as S. griseus (the strain I'm using does not produce streptomycin). Can you suggest anything that would be especially interesting? Without knowing anything about it, I thought of lavendulae, coelicolor, venezuelae, and aureofaciens. If these sporulate well, and aren't too finicky in their growth, can the NRRL supply me with authentic cultures?

I have been reading your group's work on hydroxystreptomycin. I take it that streptomycin-resistant mutants would also be resistant to the new agent. For our genetic work, we badly need an antibiotic with the general properties of streptomycin (with respect to occurrence of resistant mutants in one step) but which does not show cross-resistance with sm. None of the few things we've tried so far has been very satisfcatory.

Your note on culture collections in the USDA Yearbook bethkened that you or your colleagues might be able to evaluate a suggestion for a new approach to this problem. We've been sweating over this sort of thing ourselves, of course, with about 2000 mutants, etc., to keep watch over, and more every day. We have been using the "simplified" technique (suggested by A.D. Hershey) of distilling the moisture in our samples through a cotton plug to $CaCl_2$ in a glass tube sealed off under vacuum. This is not too bad, but cumbersome, and tends to give mechanically weak ampoules.

I wondered first of all about three points: 1) Is air (as distinguished from moisture) deletrious to a dry culture? 2) Is freeze drying intrinsically better than drying at room temperature from a low-electrolyte menstrum? 3) Why not dry the cells directly on an inert dessicant?

If we knew more aboutbthe biophysics of the lyophil technique-- for example, what is the vapor pressure of water over a properly preserved specimen, at equilibrium?--- it would be easier to solve the problem in a simple way, and someone really ought to go into this from a theoretical, basic point of view. But I have been trying the following:elaborate technique:

Suspend cells in peptone. Add about 1:20 to a tube containing silica gel (previously baked). Seal off tube. (no vacuum).

This has worked reasonably well, but there is too high a rate of steady loss to be reliable for storage of more than a year. But the principle is, I think,unassailable-- mainly because of the limits of the theoretical information. I would be surprised if the method could not be empirically perfected: there are, fortunately, only two variables-- the proportion of fluid to dessicant, and the composition of the suspending fluid. In its present form, the method is very convenient for mailing cultures: I enclose an E. coli specimen some months old. Do you think any group in the NRRL (or elsewhere) would be interested in following up this suggestion? I don't have the kind of laboratory organization to do this kind of applied research, or for that matter, the biophysics that should underly it.

We haven't done much more with lactase lately. Some French workers have been following the same lines, tooth and nail. I expect one of my students will be resuming this work before long, however. My wife and I have a paper in press (J. Bact, Jan. '52) on the use of velvet in microbiology that I hope will amuse you as much as it did us.

Sincerely,

Joshua Lederberg
(Associate Professor of Genetics)